II. REMARKS

Preliminary Remarks

Amendment of the specification

(1) The paragraph beginning on page 11, line 4, of the specification is amended to include in parentheses the chemical names of the detergents that are identified by common or trademarked names in the specification. The chemical names of the specified detergents were well-known by persons skilled in the art at the time of filing.

The specification identifies TWEEN 80 as sorbitan-mono-9-octadecenoate-poly(oxy)-l,2-ethanediyl (see p. 11. line 6). At the time of filing, the chemical names of the related detergents TWEEN 20, TWEEN 40, and TWEEN 60 were well-known to be, respectively, polyoxyethylenesorbitan monolaurate, polyoxyethylenesorbitan monopalmitate, and polyoxyethylenesorbitan monostearate (for example, see Crispens et al., "Evaluation of the anticancer activities of Tweens 20, 40 and 60 in SJL/J mice," Anticancer Res., 1991, 11(1):407-8; (Ref. NR of the IDS filed 12/12/05).

ZWITTERGENT 3-12 was well-known at the time of filing to be N-dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate (*e.g.*, see Miller et al., "The Purification and Characterization of the Cytochrome d Terminal Oxidase Complex of the Escherichia coli Aerobic Respiratiry Chain," J. Biol. Chem., 1983, 258(15):9159-9165; see page 9159, right column at bottom, Ref. AAR of the IDS filed 12/12/05). The name ZWITTERGENT in the paragraph (p. 11, line 7) is re-written in capital letters, pursuant to M.P.E.P. §608.01(v).

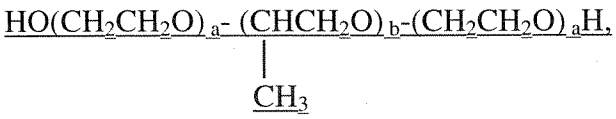
TEEPOL HB7 was well-known at the time of filing to be alkyl (C9-C13) sodium sulfates (*e.g.*, see column 10 of U.S. Patent No. 5,932,212, of Khalaf, which was filed May 24, 1996; Ref. DR of the IDS filed 12/12/05).

SPAN 85 was well-known at the time of filing to be sorbitan trioleate (*e.g.*, see Blondino et al., "The quantitative determination of aspirin and its degradation products in a model solution aerosol," J. Pharm. Biomed. Anal., 1995, 13(2):111-9; Ref. IR of the IDS filed 12/12/05).

(2) The paragraph beginning on page 11, line 10, of the specification is amended to include chemical descriptions of PEG 1000 and the block polymer surfactant PLURONIC L121 (poloxamer 401).

At the time of filing, PEG 1000 was well-known to refer to polyethylene glycol having average molecular weight of 1000 (*e.g.*, see Morris et al., "Structural properties of polyethylene glycol-polysorbate 80 mixture, a solid dispersion vehicle," 1992, J. Pharm. Sci. 81(12):1185-8, Ref. EER of the IDS filed 12/12/05).

Chemical descriptions of block polymer surfactants such as PLURONIC L121 (poloxamer 401) are found in Schmolka ("A Review of Block Copolymer Surfactants," J. Am. Oil. Chem. Soc., 1977, 54:110; Ref. JJR of the IDS filed 12/12/05) and Hunter et al. ("The Adjuvant Activity of Nonionic Block Polymer Surfactants," J. Immunol., 1981, 127(3):1244; Ref. RR of the IDS filed 12/12/05), both of which were cited in the present application (page 11, lines 15-16). The paragraph beginning on page 11, line 10, is amended to specify that the block polymer surfactants identified in the specification are called block polymers because they contain polyoxypropylene (POP) and polyoxyethylene (POE) portions which occur in separate blocks, as described on page 1245 of Hunter et al. (top of right column). The same paragraph is further amended to describe the chemical structure of the block co-polymer PLURONIC L121 (poloxamer 401) as having the general structure: $(POE)_a$- $(POP)_b$- $(POE)_a$, as shown below:



wherein a and b are such that the average molecular weight of the polyoxypropylene blocks in the molecule is 4000, and approximately 10% of the molecular weight of the copolymer is composed of the polyoxyethylene blocks. This chemical description of PLURONIC L121 (poloxamer 401) is the same as that given in Figure 1 and in the bridging paragraph on page 110 of Schmolka, which describes the chemical structure of the poloxamer surfactants, and in Table 1 on page 112 of Schmolka, which describes the physical characteristics of poloxamer 401. The same description of the chemical structure and characteristics of PLURONIC L121 (poloxamer 401) is also given in Figure 1 on page 1245 of Hunter et al. (1981). A clerical error in the citation of the

Hunter et al. (1981) reference on line 16 of page 11 that incorrectly identified the volume as vol. 129 instead of vol. 127(3) is also corrected by the amendment.

Amendment of the specification

Claims 38-46 are canceled, and new claims 47-68 are submitted. Claims 47-68 are pending. The new claims do not introduce new matter.

Claim 47 is directed to a method for enhancing an antigen-specific cytotoxic T cell lymphocyte response against cancer cells in a patient in need thereof, comprising administering:

(a) an adjuvant formulation comprising a human papillomavirus E7 protein that is capable of inducing a cytotoxic T cell lymphocyte response specific for the human papillomavirus E7 protein; and

(b) a therapeutically effective amount of at least one agent that is capable of neutralizing, blocking, antagonizing, or down regulating the activity or preventing activation of transforming growth factor β).

Claims 48, 49 and 66 identify specific TGFβ-neutralizing agents described in the specification, *e.g.*, on page 4, lines 22-24.

Claims 52-65 specify administering the tumor-associated antigen in an adjuvant formulation described in the specification, *e.g.*, on pages 10-12.

Patentability Remarks

35 U.S.C. §112, First Paragraph, Enablement

Claims 38-43, 45, and 46 were rejected under 35 U.S.C. §112, first paragraph, because the specification is considered to be enabling for a method for enhancing an antigen-specific cytotoxic T-lymphocyte response in a subject in need thereof comprising administering an antagonist of TGFβ in conjunction with the papillomavirus E7 protein or melanoma tumor associated antigens, but allegedly is not enabling in its full scope as written.

Applicants respectfully submit that the specification enables one of skill in the art to make and use the invention of claims 38-43, 45, and 46, in compliance with 35 U.S.C. §112, first

paragraph, and reserve the right to pursue claims directed to the subject matter of these claims in a continuing application. However, in the interest of expediting prosecution of the present application, the rejected claims are canceled and replaced by new claims 47-68, which are directed to a method which is described and enabled by the specification, as acknowledged in the statement of the rejection. New claim 47 and dependent claims 48-68 are directed to a method for enhancing an antigen-specific cytotoxic T cell lymphocyte response against cancer cells in a patient in need thereof, comprising administering:

(a) an adjuvant formulation comprising a human papillomavirus E7 protein that is capable of inducing a cytotoxic T cell lymphocyte response specific for the human papillomavirus E7 protein; and

(b) a therapeutically effective amount of at least one agent that is capable of neutralizing, blocking, antagonizing, or down regulating the activity or preventing activation of transforming growth factor β.

Withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

35 U.S.C. §112, Second Paragraph

Claims 38-45 were rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting a step that facilitates an antigen-specific CTL response.

Claim 45 was further rejected under 35 U.S.C. §112, second paragraph, because the expression "the antigen" was considered to lack antecedent basis.

Applicants submit that new claims 47-68 submitted in place of claims 38-45 are not subject to the above rejections under 35 U.S.C. §112, second paragraph. Withdrawal of the rejections under 35 U.S.C. §112, second paragraph, stated in the official action, is therefore respectfully requested.

35 U.S.C. §102(b)

Claims 38-40 and 46 were rejected under 35 U.S.C. §102(b), as being anticipated by International Patent Publication No. WO 94/09815 of Segarini et al. (1994). Publication WO 94/09815 describes a method for increasing the method of increasing the effectiveness of a

vaccine comprising administering the vaccine in conjunction with a TGF-ss-binding receptor fragment to increase the immune response to the vaccine in the individual.

To anticipate a claim, a reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). *See* the Manual for Patent Examining Procedure (M.P.E.P.), §2131.

New claims 47-68 are directed to a method for enhancing an antigen-specific cytotoxic T cell lymphocyte response against cancer cells, which comprises administering:

(a) an adjuvant formulation comprising a human papillomavirus (HPV) E7 protein that is capable of inducing a cytotoxic T cell lymphocyte response specific for the HPV E7 protein; and

(b) a therapeutically effective amount of at least one agent that is capable of neutralizing, blocking, antagonizing, or down regulating the activity or preventing activation of transforming growth factor β.

The WO 94/09815 publication does not describe a method that comprises administering an adjuvant formulation comprising a HPV E7 protein that is capable of inducing a cytotoxic T cell lymphocyte response specific for the HPV E7 protein, in conjunction with a TGFβ antagonist, as specified in the current claims. Accordingly, withdrawal of the rejection of the claims under 35 U.S.C. §102(b), as being anticipated by WO 94/09815 is respectfully requested.

Claims 38-39, 42-43, and 45-46 were rejected under 35 U.S.C. §102(e), as being anticipated by U.S. Patent Application No. 2002/0004052 of Berd et al. (1995).

Berd et al. describes a method for treating cancer comprising administering a tumor-associated antigen in conjunction with cyclophosphamide. Berd et al. does not describe a method comprising administering an adjuvant formulation comprising a HPV E7 protein that is capable of inducing a cytotoxic T cell lymphocyte response specific for the HPV E7 protein, in

conjunction with a TGFβ antagonist, as specified in the current claims. Applicants respectfully request that the rejection of the claims under 35 U.S.C. §102(b), as being anticipated by Berd et al. (1995) be withdrawn.

III. IN CONCLUSION

All rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a Notice to that effect is earnestly solicited. If the examiner identifies any points that he feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

No official fees are believed to be due, however, please charge any fees associated with the submission of this response to Deposit Account Number 03-3975.

Respectfully submitted,

Date: June 30, 2006

By_____

Thomas A. Cawley, Jr., Ph.D.
Reg. No. 40944
Tel. No. 703.770.7944
Fax No. 703.770.7901

PILLSBURY WINTHROP SHAW PITTMAN LLP
P.O. Box 10500
McLean, VA 22102
703.770.7900